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EXAMINER	
WHALEY, PABLO S	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/634,145	HENG ET AL.	
	Examiner	Art Unit	
	PABLO WHALEY	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 January 2011*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15,17-26 and 28-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15,17-26 and 28-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's arguments, filed 01/04/2011, have been fully considered.

The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Applicant has not filed any amendments to the claims.

Status of Claims

Claims 1-15, 17-26, and 28-30 are pending and under consideration.

Claims 16 and 27 are cancelled.

Claim rejections - 35 USC § 112, 2nd Paragraph

Response to Arguments

Applicant's arguments, filed 01/04/2011, have been fully considered but are not persuasive for the following reasons.

Claim rejections - 35 USC § 112, 2nd Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.
>
> The essential inquiry pertaining to this requirement is whether the claims set out and circumscribe a particular subject matter with a reasonable degree of clarity and particularity. Definiteness of claim language must be analyzed, not in a vacuum, but in light of: (A) The content of the particular application disclosure; (B) The teachings of the prior art; and (C) The claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made.

Claims 1-15, 17-26, and 28-30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims that depend directly or indirectly from claim 1, 21, and 28 are also rejected due to said dependency.

The following rejections are maintained for the reasons discussed below.

Claims 1 and 21 recite "calculating, for each of said sets, a deviate of a predicted risk from an indicator of disease state for the set, said predicted risk using said candidate model and non-genetic data in that set" (see lines 13-15). It is unclear what data is used for calculating disease risk. It is unclear what is meant by "for each of said sets". Are deviates calculated for the claimed non-genetic, indicator of disease status data, and genetic data sets? Clarification is requested. This rejection could be overcome, for example, by amending the claims to recite "calculating a deviate of predicted risk using an indicator of disease status and non-genetic data." The applicant is encouraged to introduce mathematical equations including relevant parameters.

In response to applicant's argument that non-genetic data and indicator of disease status data are intended to be used in the calculation of the deviate, this intention is not reflected in the claims. Therefore this rejection is maintained.

Claims 1 and 21 recite "calculating a sum of weighted deviates for all said sets" (see lines 16-20). As the claims previously recite a plurality of sets of data including non-genetic data, genetic data, and an indicator of disease status (lines 3-5), it is unclear what data is used for calculated a sum of weighted deviates. Clarification is

requested. This rejection could be overcome, for example, by amending the claims to recite "calculating a sum of weighted deviates using genetic data." The applicant is encouraged to introduce mathematical equations including relevant parameters.

In response to applicant's argument that genetic data is intended to be used in the calculation of the sum of weighted deviates, this intention is not reflected in the claims. Therefore this rejection is MAINTAINED.

Claim Rejections - 35 USC § 103

Response to Arguments

Applicant's arguments, filed 01/04/2011, have been fully considered.

Applicant's remarks states for the record that the claimed model is intended to calculate predicted risk as a function of non-genetic and indicator of disease status data; that deviates are calculated using the predicted risk and indicator of disease status data; that sum of weighted deviates are calculating using genetic data; and that the process for determining weights has a constraint that data sets in each group have like genetic data (i.e. the same) and that weights associated with the data sets are the same [see Remarks, page 2 and 3]. As noted above, see 112 2nd rejections, the instant claims do not specifically recite these intended limitations and applicant has not filed any amendments to the claims.

In response to applicant's argument that the cited prior art does not teach "fitting" based on the calculation of the deviate and the sum of weighted deviates using genetic data, it is admitted that the cited prior art of Walter does not recite this limitation but the

claims do not explicitly require calculation of the deviate and the sum of weighted deviates using genetic data. However, after further consideration and in view of applicant's arguments, the rejections are withdrawn and a new ground of rejection has been applied. The prior art of Jacob has been cited to address this limitation, as set forth below. Applicant's additional arguments regarding Shattuck-Eidens, Pharaoh, Nelson, and Marshall are moot in view of the new ground of rejections.

NEW GROUND OF REJECTIONS

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The factual inquiries set forth in Graham v. John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-3 and 17-21 are rejected under 35 U.S.C. 103(a) as being made obvious by Jacob (US 6,162,604, Issued Dec. 19, 2000), in view of Shattuck-Eidens et al. (JAMA, 1997, 278 (15): 1242-1250), and in view of Pharaoh et al. (Nature Genetics; May 2002, 31: 33-36).

CLAIM SUMMARY

The claims are directed to a method, program, and system for determining a statistical model for predicting disease risk for a member of a population. The claims require collecting a plurality of data sets associated with a member of a population. The data includes non-genetic data, genetic data indicative of the presence or absence of a genetic marker in a member of a population, and indicators of disease status. A candidate statistical model is created for calculating disease risk as a function of non-genetic data, wherein the model depends on a plurality of parameters. These model parameters are optimized by calculating deviates using the predicted risk and the indicator of disease status, and calculating the sum of weighted deviates using genetic data. The process for determining weights has a constraint that data sets in each group have like genetic data (i.e. the same) and that weights associated with the data sets are the same.

PRIOR ART

Jacob teaches a method for predicting autoimmune disease using genetic markers. The method requires obtaining genetic data from patient samples indicative of the presence or absence of the disease [Ref. claim 1 and Col. 3]. Regression models

are used to determine associations between genetic data and the presence of specific disorders [Col. 5, Example 3]. Optimization of regression models is performed to assess whether pair wise interactions improved the model fit compared to a second model [Col. 3, ¶2]. Odds values are calculated as indicators of disease risk in individuals [Col. 3, ¶2]. Disease risk is calculated by determining a departure from multiplicative model [Example 5]. Jacob obtains ethnicity data from individuals, as well as sex and age data [Col. 6], which reads on collecting non-genetic data.

Jacob does not teach a disease risk model that is a function of non-genetic data, wherein the model depends on a plurality of parameters, as in claims 1 and 21.

Jacob does not teach calculating disease risk as a function of non-genetic data, and optimizing model parameters by calculating deviates using the predicted risk and the indicator of disease status, and calculating the sum of weighted deviates using genetic data, wherein weights associated with the data sets in a group are the same, as in claims 1 and 21.

Shattuck-Eidens teaches a method for predicting the presence of harmful genetic mutations in individuals [see p.1243, Col. 3, p.1244, Col. 1 and 2, and p.1246, Col. 3]. In particular, non-genetic data and indicators of disease status is collected [p.1243-1244 and p.1246, Col. 2 and 3]. Data is obtained for genetic markers indicative of the early onset of breast cancer [Tables 2, 3, and 4, and p.1249, Col. 2], which shows genetic markers indicative of the presence of disease. The probability of carrying a genetic mutation is calculated using a regression model that is a function of non-genetic data and parameters; see p. 1243, Col. 3]. Optimization is performed by fitting model

parameters based on additive scaled deviance calculations; see p. 1243, Col. 3 and p.1244, Col. 3, which is interpreted as fitting of model parameters by calculating a sum of weighted deviance of a predicted risk. The fitting process includes adding factors (i.e. weights) that reduce scaled deviance at each step; see p. 1244, Col. 3, which suggests weights associated with genetic data. Furthermore, groups with the same disorder are assigned a similar integer value [p.1246, Col. 2 and 3], which reasonably suggest a constraint such that sets with the same genetic data have the same weights. The above analyses are performed using a software package; see p.1244, Col. 2, which shows collecting data by a computing device, and an article of manufacture and system for performing the above method steps.

Pharaoh teaches a statistical model for predicting cancer risk. In particular, Pharaoh shows collecting genetic and non-genetic risk factor data (i.e. genetic and non-genetic data); see Abstract, p.35, Col. 1, and Table 1. Polygenic models for predicting risk in a population are fitted to the population data; see pages 33-34. The models determine the risk of breast cancer conferred by single genes; see Table 1 and p. 35, Col. 2, which shows genetic data indicative of the presence or absence of genetic markers.

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to have modified the method of Jacob by calculating disease risk as a function of non-genetic data and other parameters, with a reasonable expectation of success, since one of skill in the art would recognize that the analysis of non-genetic data could be carried out using any known statistical techniques, such as fitting non-

genetic data to the survival model of Shattuck-Eidens, as set forth above, and in view of Pharaoh, who teaches risk models that use non-genetic and genetic risk factor data, as set forth above. The motivation to combine genotype and non-genotype risk factors would have been to provide risk discrimination that has practical value for health care, as suggested by Pharaoh; see page 35, Col.2.

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to have modified the method made obvious by Jacob and Shattuck-Eidens by optimizing model parameters by calculating deviates using data for predicted risk and indicator of disease status, as taught by Shattuck-Eidens, with a reasonable expectation of success, since one of skill in the art would recognize that parameter optimization using deviates could be carried out using any known statistical techniques, such as those taught by Shattuck-Eidens, above. The motivation would have been to improve model fit, as suggested by Jacob and Shattuck-Eidens.

Jacob and Shattuck-Eidens do not specifically teach calculating the sum of weighted deviates using genetic data, as in claims 1 and 21. However, Jacob suggests this limitation by teaching the optimizing of regression models using genetic data, and since one skilled in the art would recognize that the optimization of regression models inherently requires sum of weighted deviate calculations.

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to have modified the method made obvious by Jacob and Shattuck-Eidens by determining weights under the constraint that data sets in each group have like genetic data (i.e. the same) and that weights associated with the data

sets are the same, with a reasonable expectation of success, in view of Shattuck-Eidens, who teaches scaled deviance calculations, which inherently include weights, and since Shattuck-Eidens suggests groups with the same disorder assigned a similar weight. The motivation would have been to account for model bias by reducing scaled deviance values associated with different groups, as suggested by Shattuck-Eidens, page 1244, col. 3.

Claims 4, 5, and 23-26 are rejected under 35 U.S.C. 103(a) as being made obvious by Jacob (US 6,162,604, Issued Dec. 19, 2000), in view of Shattuck-Eidens et al. (JAMA, 1997, 278 (15): 1242-1250), and in view of Pharaoh et al. (Nature Genetics; May 2002, 31: 33-36), as applied to claims 1-3, 17-21, and further in view of Nelson et al. (J Clin Epidemiol, 1998, Vol. 51, No. 3, pp. 199–209), and Marshall et al. (Statistics in Medicine; 1986;5:517-526).

Jacob, Shattuck-Eidens, and Pharaoh make obvious a method and program for determining a statistical model for predicting disease risk, as set forth above.

Jacob, Shattuck-Eidens, and Pharaoh do not teach grouping collected data such that all sets of data have like genetic data, one of said group being a reference group, and determining a group weight for each group, wherein the group weight is between 0 and 1, as in claims 4 and 5.

Jacob, Shattuck-Eidens, and Pharaoh do not teach dividing sets of data into two or more groups depending on data indicative of non-genetic factors, determining if a

criterion is met after dividing, and regrouping sets of data back into one group when criterion is not met, as in claim 23-26.

Nelson teaches method of recursive partitioning for the identification of disease risk groups; Abstract. Individual groups of data are split by recursive partitioning in order to identify variables that minimize the variance between the subsets; see p.201-202 and Fig. 1. Classification tree models are constructed and an optimum sized model is selected using cross-validation; see p.201, Col. 1 and Col. 2. The method requires fitting dummy variables with conditional logistic regression to estimate odds ratio's (i.e. group weights) for subsets in a classification tree; see p.204, Col. 2. Each subset that is partitioned in classification tree is assigned an index value based on a weighted average; see Appendix A, which is interpreted as an alternative teaching for group weights between 0 and 1; see p.207, Col. 2. The partitioning of data is based on all of different risk factor groups involved in the study; e.g. case and control data, see p.202 and Fig. 1. An optimized tree is obtained as a result of partitioning, pruning, and cross-validation, and that classification tree risk subgroup can also be modeled via conditional regression analysis, which inherently include optimization of model parameters by minimizing of target functions; see page 204, Col. 1, and Col. 2. The motivation would have been to allow effect estimates to be adjusted for matching variables; p.204, Col. 1.

Marshall teaches methods of recursive partitioning of data. In particular, Marshall teaches combining partitions based on search criteria; see p.522, which is interpreted as regrouping data. The benefit of this method is to obtain optimal partitions. Group data is assigned to binary values; e.g. 0 and 1; see page 518-519.

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to have grouped data such that all sets have the same genetic data and one of said groups is a reference group, in the method made obvious by Jacob, Shattuck-Eidens, and Pharaoh, with a reasonable expectation of success, in view of the teachings of Pharaoh, who shows groups that are susceptible to different genetic factors have different probabilities of risk; see page 34, Col. 1, and since Nelson shows the probabilities can be predictably determined for case and control groups, see p.201, Col. 2. The motivation would have been to minimize the variation in predicted risk, as suggested by Pharaoh, p.34, Col. 1.

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to have determined group weights, wherein weights are between 0 and 1, in the method made obvious by Jacob, Shattuck-Eidens, and Pharaoh, with a reasonable expectation of success, since Nelson and Marshall both show methods for partitioning data into groups assigning binary values (i.e. weights) to the groups, as set forth above. The motivation would have been to uncover interactions between variables that may be overlooked in the traditional application of logistic regression to case-control data, as suggested by Nelson; Summary and p. 208, Col. 1.

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to have optimized group weights by minimizing a target function that is dependent on a plurality of residuals, in the method made obvious by Jacob, Shattuck-Eidens, and Pharaoh ,with a reasonable expectation of success, since Nelson shows fitting variables with conditional logistic regression to estimate odds ratio's (i.e.

group weights) with predictable results, as set forth above, which suggests optimizing group weights by minimizing a target function. The motivation would have been to improve results through standard methods of model optimization, as suggested by Nelson; see p. 201.

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to have divided sets of data into two or more groups depending on data indicative of non-genetic factors, and determined if a criterion is met after dividing, in the method made obvious by Jacob, Shattuck-Eidens, and Pharaoh, with a reasonable expectation of success, since Nelson shows dividing non-genetic data into groups (i.e. case and control) based on a numerical criterion, and repeats the partitioning process for all subgroups after the division process; see p.201, Col. 2. The motivation would have been to perform routine optimization for identifying the variable that gives the best separation of case and control groups, as suggested by Nelson; p.208, Col. 1.

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to have regrouped sets of data back into one group when criterion is not met, in the method made obvious by Jacob, Shattuck-Eidens, and Pharaoh, with a reasonable expectation of success, since Marshall shows recursive partitioning of data by combining partitions based on search criteria; see p.522, which is interpreted as regrouping data. The motivation would have been to obtain optimal partitions in statistical models, as suggested by Marshall, above.

Claims 6, 7, 8, 9, 10, and 11 are rejected under 35 U.S.C. 103(a) as being made obvious by Jacob (US 6,162,604, Issued Dec. 19, 2000), in view of Shattuck-Eidens et al. (JAMA, 1997, 278 (15): 1242-1250), and in view of Pharaoh et al. (Nature Genetics; May 2002, 31: 33-36), in view of Nelson et al. (J Clin Epidemiol, 1998, Vol. 51, No. 3, pp. 199–209), and in view of Marshall et al. (Statistics in Medicine; 1986;5:517-526), as applied to claims 1-3, 17-21, and further in view of Parzen et al. (Biometrics, 1999, 55, 580-584).

Jacob, Shattuck-Eidens, Pharaoh, Nelson, and Marshall make obvious a method and program for determining a statistical model for predicting disease risk, as set forth above.

Jacob, Shattuck-Eidens, Pharaoh, Nelson, and Marshall do not teach minimizing a target function dependent on residuals and weights, as in claims 6, 7, and 8.

Jacob, Shattuck-Eidens, Pharaoh, Nelson, and Marshall do not teach data indicative of time or using a Cox hazard model, as in claims 9 and 10.

Parzen teaches a Cox hazard regression model for calculating disease risk in a subject based on non-genetic data as a function of time [Section 2, Table 1, Table 2, and p.581, Col. 2]. Parzen calculates partial risk estimates using a Cox likelihood score vector based on a sum of weighted averages and a binary variable between 1 and 0 (i.e. weight) [p.581, Col. 2, Equation 2], which is interpreted as a minimizing a target function. Model parameters are optimized by data fitting [Section 3], and using a residual equation for calculating goodness of fit [p.582, Col. 2].

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to have minimized a target function dependent on residuals and weights, as taught by Cleveland, above, in the method made obvious by Jacob, Shattuck-Eidens, Pharaoh, Nelson, and Marshall, with a reasonable expectation of success, since Parzen also teaches optimization of regression model parameters, as set forth above. The motivation would have been to improve model accuracy using an alternative scoring statistic, as suggested by Parzen; p.582, Col. 2.

It would have been obvious for one of ordinary skill in the art at the time of the instant invention to have provided a predictable variation of the type regression model used, such as the Cox hazard regression model taught by Parzen, in the method made obvious by Jacob, Shattuck-Eidens, Pharaoh, Nelson, and Marshall, with a reasonable expectation of success, in view of the rationale for a *prima facie* case of obviousness provided by the Supreme Court in *KSR International Co. v. Teleflex Inc.*, 550 U.S. 398 (2007). See MPEP 2143. In this case, the rationale would have been the simple substitution of one known method of predicting risk for another, such as a Cox regression model, since these variations are predictable to one of ordinary skill in the art. For these reasons, the instant claims do not recite any new element or new function or unpredictable result.

Claims 12 and 22 are rejected under 35 U.S.C. 103(a) as being made obvious by Jacob (US 6,162,604, Issued Dec. 19, 2000), in view of Shattuck-Eidens et al. (JAMA, 1997, 278 (15): 1242-1250), in view of Pharaoh et al. (Nature Genetics; May 2002, 31:

33-36), in view of Nelson et al. (J Clin Epidemiol, 1998, Vol. 51, No. 3, pp. 199–209), and in view of Marshall et al. (Statistics in Medicine; 1986;5:517-526), as applied to claims 1-3, 6-11, 17-21, and further in view of Raghunathan et al. (Survey Methodology, 2001, 27(1):85-95).

Jacob, Shattuck-Eidens, Pharaoh, Nelson, and Marshall make obvious a method and program for determining a statistical model for predicting disease risk, as set forth above.

Jacob, Shattuck-Eidens, Pharaoh, Nelson, and Marshall do not teach imputing missing data, as in claims 12 and 22.

Raghunathan teaches a method for imputing missing data into a statistical model; see Abstract, Section 3, p.89, Col. 1. Regression is performed for a data set that has missing data under a constraint that a subpopulation is the same; see p.89, Col. 1. The logistic regression model is then fitted to each imputed data set to obtain maximum likelihood estimates of the regression coefficients and asymptotic covariance matrices; see p.89, Col. 2. The method uses "multiply imputed estimates" of the regression coefficients calculated as a ratio; see p.89, Col. 2, which is interpreted as determining adjustment factors under a constraint.

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to have imputed missing data into a model, as taught by Raghunathan, above, in the method made obvious by Jacob, Shattuck-Eidens, Pharaoh, Nelson, and Marshall, with a reasonable expectation of success, since

Shattuck-Eidens shows grouping of data; see p. 1244, Col. 3, and suggests the existence of incomplete data sets; Table 5 and p.1248, Col. 2. The motivation would have been to improve model accuracy when data is missing at random, as suggested by Raghunathan [Abstract].

Claims 13-14 are rejected under 35 U.S.C. 103(a) as being made obvious by Jacob (US 6,162,604, Issued Dec. 19, 2000), in view of Shattuck-Eidens et al. (JAMA, 1997, 278 (15): 1242-1250), in view of Pharaoh et al. (Nature Genetics; May 2002, 31: 33-36), in view of Nelson et al. (J Clin Epidemiol, 1998, Vol. 51, No. 3, pp. 199–209), in view of Marshall et al. (Statistics in Medicine; 1986;5:517-526), and in view of Raghunathan et al. (Survey Methodology, 2001, 27(1):85-95), as applied to claims 1-3, 6-12, 17-22, and further in view of Pfeffermann et al. (International Statistical Review, 1993, 61, 2:317-337).

Jacob, Shattuck-Eidens, Pharaoh, Nelson, Marshall, and Raghunathan make obvious a method and program for determining a statistical model for predicting disease risk, as set forth above.

Jacob, Shattuck-Eidens, Pharaoh, Nelson, Marshall, and Raghunathan do not teach optimizing model parameters using an adjustment factor that is a function of a ratio of the number of members in a population who share the same characteristics over the total number of members in a population, as in claims 13 and 14.

Pfeffermann teaches methods for using sampling weights in statistical models. In particular, Pfeffermann discusses the use of sampling weights for estimating model parameters by fitting; see p.318, Section 4.2, and p.327. In one case, the weight represented by a step function that equates to 0 or 1 based on a particular constraint where the data is great than or equal to 0; see p.327, which shows weights based on a constraint. Samples can also be weighted using a count estimate of the form Ni/Nj, which shows an adjustment factor that is a function of a ratio of the number of members in a population who share the same characteristics over the total number of members in a population The motivation would have been to correct for disproportionality of the sample in the target population [Introduction].

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to have optimized model parameters using an adjustment factor that is a function of a ratio of the number of members in a population who share the same characteristics over the total number of members in a population, in the method made obvious by Jacob, Shattuck-Eidens, Pharaoh, Nelson, Marshall, and Raghunathan, with a reasonable expectation of success, in view of Pfeffermann, who suggests weighting data using an adjustment factor that is a function of a ratio of the number of members in a population who share the same characteristics over the total number of members in a population, and in view of the rationale for a *prima facie* case of obviousness provided by the Supreme Court in *KSR International Co. v. Teleflex Inc.*, 550 U.S. 398 (2007). See MPEP 2143. In this case, the rationale would have been to improve model fitting based on variations of known design parameters, such as using

population ratios to decrease the variance of the estimators, as suggested by Pfeffermann; see p.329, since these variations are predictable to one of ordinary skill in the art. For these reasons, the instant claims do not recite any new element or new function or unpredictable result.

Claims 28-30 are rejected under 35 U.S.C. 103(a) as being made obvious by Jacob (US 6,162,604, Issued Dec. 19, 2000), in view of Shattuck-Eidens et al. (JAMA, 1997, 278 (15): 1242-1250), and in view of Pharaoh et al. (Nature Genetics; May 2002, 31: 33-36), as applied to claims 1-3 and 17-21, and further in view of Walter et al. (American Journal of Epidemiology, 1978, 108(5): 341-6).

Jacob, Shattuck-Eidens, and Pharaoh make obvious a method and program for determining a statistical model for predicting disease risk, as set forth above.

Jacob, Shattuck-Eidens, and Pharaoh do not teach using a plurality of models and selecting the model that produces the lowest sum of weighted deviates, as in claims 28, 29, and 30.

Walter teaches methods of determining models for predicting disease risk for members of a population. In particular, Walter teaches a plurality of statistical models for predicting risk; see pages 341-343, Examples 1 and 2, and see p.345. Goodness-of-fit tests statistics (i.e. sum of weighted deviates) are used to assess model accuracy; see p.344, Col. 2. The appropriate model is determined by its ability fit data, and criteria

for defining a good fit vary according to methods used for estimating parameters; see p.346, Summary.

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to have used a plurality of disease risk models and selected the optimum model, as taught by Walter, with a reasonable expectation of success, since one of skill in the art would recognize that the analysis of multiple models could be carried out using any known statistical techniques, such goodness-of-fit techniques used by Walter, above, for the benefit of selecting the best model.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Pablo Whaley whose telephone number is (571)272-4425. The examiner can normally be reached between 11am-7pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie Moran can be reached at 571-272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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